REMARKS

Claims 1-6 are now pending.

The Examiner has rejected claims 1-6 under 35 U.S.C. § 101 for allegedly lacking patentable utility. For reasons detailed below, the rejection should be withdrawn and the claims allowed to issue.

1. The Claims Have Patentable Utility

The Examiner has rejected claims 1-6 under 35 U.S.C. § 101 for allegedly lacking patentable utility. According to the Examiner, the specification does not provide a function for *Vezf1* or its human homologue, DB1, nor compare these proteins to proteins of known function. The Examiner states that:

> "While the DNA claimed in the instant invention may be used to make protein or to test for gene expression, such a use is not of value if the function of the protein isunknown. Without a readily apparent utility for the protein, it is unclear that the purified and isolated Vezf1 gene (claim 1), the purified and isolated nucleic acid encoding the Vezf1 protein (claim 3) or the expression vector containing the DB1 gene (claim 6) have any utility."

The Examiner also distinguishes the references cited by Applicants, Xiong *et al.*, Dev. Biol. (1999) 206:123-141 ("Xiong") and Aitsebaomo *et al.*, J. Biol. Chem. (2001) 276:39197-39205 ("Aitsebaomo"). The Examiner argues that the specification does not state that *Vezf1* is restricted to vascular endothelial cells, unlike the teaching of Xiong. The Examiner distinguishes the present application from Aitsebaomo by arguing that while Aitsebaomo teaches that *Vezf1* regulates expression of the endothelin-1 promoter, the instant specification does not. The Examiner has also found the Stuhlmann declaration to be unpersuasive on similar grounds, adding that the Stuhlmann declaration "teaches endothelial cells only express Vezf1 when proliferation is required which is not described in the specification."

The Examiner also states that the present "specification and the art at the time of filing do not correlate Vezf1 expression with any vascular disease; therefore, the asserted utility is not specific to any vascular disease." The Examiner argues that present invention therefore does not have utility to diagnose or treat vascular disease.

Applicants respectfully disagree. The Examiner states that "[t]he specification and the art at the time of filing do not teach that Vezf1 expression occurs only in endothelial cells; therefore, the asserted utility is not substantial." By requiring that the specification and the art at the time of filing show that Vezf1 expression occurs only in endothelial cells, the Examiner is improperly requiring perfect utility. To show substantial utility, Applicants need only show partial success in achieving a useful result. See MPEP § 2107.01 *citing E.I. du Pont De Nemours and Co. v. Berkley and Co.*, 620 F.2d 1247, 1260 n.17 (9th Cir. 1980) ("A small degree of utility is sufficient... The claimed invention must only be capable of performing some beneficial function... An invention does not lack utility merely because the particular embodiment disclosed in the patent lacks perfection or performs crudely... In short, the *defense of non-utility cannot be sustained without proof of total incapacity.*") (emphasis added). Accordingly, Applicants need not show that *Vezf1* is absolutely restricted to only vascular endothelial cells and be capable of absolutely distinguishing vascular endothelial cells from any other cell; Applicants need only show that *Vezf1* is differentially expressed on vascular endothelial cells and some other cell type and may be used as a marker to distinguish between those cells.

The present specification clearly supports differential expression of *Vezf1* on vascular endothelial cells and other cells. The specification clearly discloses that *Vezf1* is expressed primarily in vascular endothelial cells, as cited by the Examiner, with much lower expression in some cells, and with a total lack of expression in other cells. See specification at page 41, line 8

to page 43, line 11 ("No detectable [*Vezf1*] expression was observed in either erthroid precursors in the yolk sac, in nucleated blood cells from all stages of embryos tested, or in... fetal liver other than what appeared to be the endothelial linings of capillaries."). The specification also provides further support that different cell types have differential expression of *Vezf1*. See specification at page 43, line 13 to page 45, line 3 . Based upon this disclosure, a person of ordinary skill in the art would recognize that *Vezf1* may be used as a marker to distinguish vascular endothelial cells from other cells which lack expression of *Vezf1*, such as hematopoetic cells, erthroid precursors, nucleated blood cells, and non-vascular endothelial liver cells. A person of ordinary skill in the art would also recognize that *Vezf1* may be used to differentiate between different cell types based upon the differences in expression of *Vezf1,* because differences in expression levels between cell types would still have identifying value. Accordingly, by providing evidence of the usefulness of *Vezf1* to distinguish vascular endothelial cells from some types cells, Applicants have demonstrated a substantial utility.

Contrary to the Examiner's assertion, Xiong and Aitsebaomo support the asserted utility by teaching that *Vezf1* is specific to vascular endothelial cells. The asserted utility resides in *Vezf1*'s endothelial specificity, rather than its molecular function. Accordingly, Xiong and Aitsebaomo are cited for their corroboration of the disclosure in the present specification that Vezf1 is primarily limited to vascular endothelial cells. See, e.g., specification at page 43, lines 12-16 ("The data therefore indicates that *Vezf1* expression is mainly confined to vascular endothelial cells and their precursors rather than hematopoietic cells."). Furthermore, Applicants respectfully submit that the Examiner is mistaken in his assertion that Xiong and Aitsebaomo cannot be used to support the present application, as they were unavailable at the time of filing. It is proper to submit evidence that corroborates what is disclosed in the specification, even if the

corroborating references come after the time of filing. See *Knoll Pharmaceutical Co. v. Teva Pharmaceuticals USA, Inc.*, 367 F.3d 1381, 1385 (Fed. Cir. 2004) ("Evidence developed after the patent grant is not excluded from consideration, for understanding of the full range of an invention is not always achieved at the time of filing the patent application.").

Applicants also disagree with the Examiner's argument that the specification does not provide sufficient evidence of the specificity of *Vezf1* to vascular endothelial cells or its utility to treat vascular disease. Applicants are not required to prove restriction of *Vezf1* to vascular endothelial cells with absolute certainty; Applicants need only show that there is a reasonable correlation between the activity in question and the asserted utility. See MPEP § 2107.02 ("[T]he applicant does not have to provide evidence sufficient to establish that an asserted utility is true 'beyond a reasonable doubt....' Nor must an applicant provide evidence such that it establishes an asserted utility as a matter of statistical certainty.... Instead, evidence will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true.") (emphasis in original). Thus, Applicants need only show that it is more likely than not true that *Vezf1* is primarily associated with vascular endothelial cells and may be used as a marker or to treat vascular disease.[1] The specification and working examples in the specification are clearly directed to angiogenesis and the vascular system, and the examples also provide substantial evidence of the specificity of *Vezf1* to vascular endothelial cells. See, e.g., specification at pages 41, line 7 to page 43, line 16. Applicants have also provided a declaration from a person of ordinary skill in the art which concludes that, based on the disclosure of the present application, *Vezf1* is "a marker specific for adult endothelial cells

[1] Applicants also note that it is not required that all utilities be proven. See MPEP § 2107.02 ("[A]n applicant need only make one credible assertion of specific utility for the claimed invention to satisfy 35 U.S.C. 101 and 35 U.S.C. 112; additional statements of utility, even if not "credible," do not redner the claimed invention lacking in utility.").

which is expressed normally in the endothelial cell lining of capillary networks and mature vessels throughout adult tissues." See Stuhlmann Declaration at para. 3. Based upon the disclosure of the present application, and further supported by the Stuhlmann Declaration, a person of ordinary skill in the art would conclude that it is more likely than not that *Vezf1* is primarily restricted to vascular endothelial cells.

Based upon the foregoing arguments, Applicants submit that the present specification and state of the art at the time of filing provide more than adequate evidence to prove substantial utility for the present invention. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn.

CONCLUSION

Entry of the foregoing remarks into the file of the above-identified application is respectfully requested. The Applicant believes that the invention described and defined by claims 1-6 are patentable over the rejection of the Examiner. Withdrawal of the rejection and reconsideration of the claims is requested. An early allowance is earnestly sought.

Respectfully submitted,

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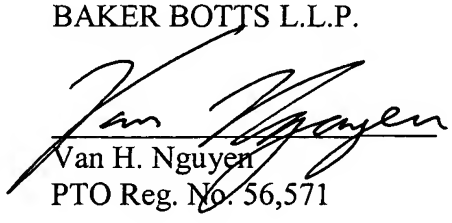

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